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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/311,720	05/14/1999	GREGORY M. GLENN	PM254809	1614

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/311,720	GLENN ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *32-34,37,38,42,43,47-54 and 62-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99 and 102-136* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,4,9-12,14,28,30-44,47-54,62-74,80,81,87,90,93-96,98,99 and 102-136.

DETAILED ACTION

This application is a continuation-in-part of 08/749,164, filed November 14, 1996, now US Patent 5,910,306, which claims benefit to provisional application 60/086,196, filed My 21, 1998.

Applicants amendment filed July 15, 2004, has been received and entered. Claims 3, 5-8, 13, 15-27, 29, 45, 46, 55-61, 75-79, 82-86, 88, 89, 91, 92, 97, 100 and 101 are canceled. Claims 128-136 have been added. Claims 1, 2, 32-34, 37, 38, 42, 43, 47-54, 80 and 93 have been amended. Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 62-74, 80, 81, 87, 90, 93-96, 98, 99, and 102-136 are pending.

Election/Restriction

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 62-74, 80, 81, 87, 90, 93-96, 98, 99 and 102-136 are pending. Claims 62-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of adjuvant, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement. Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99 and 102-136 are currently under examination as they are drawn to the species CpG as an adjuvant.

Priority

Applicants summarize Examiners basis for denying priority and argue that the generic claims are entitled to at least the priority date of July 17, 1997, the filing date of 08/896,085 (US

Patent 5,980,898) . Applicants note literal support for the use of bacterial DNA (column 11, line 37) and the use of "nucleic acid(s) contained in the formulation may encode the antigen, the adjuvant or both" (column 14, lines 13-29). Applicants argue that this provides literal support for the instant claims. See Applicants amendment, page 17. Applicants' response and arguments have been fully considered, and not found persuasive. Initially it is noted that column 11 only supports nucleic acid sequences that "may encode" the adjuvant not the use of the nucleic acid sequence itself as an adjuvant. The literal support for the use of bacterial DNA is noted, however this was presented only in the context of activating Langerhans cells, and does not provide any specific guidance to what bacterial DNA is required, or support for the use of any other DNA as an adjuvant. Importantly, the teachings of the priority documents relied upon by Applicants fails to provide literal support for the elected invention of generally using a CpG, or any of the specific forms of CpG recited in the claims (for example CpG1 in claim 4). Moreover, the priority document fails to provide the specific support for the specific combination of using a bacterial DNA and a non-bacterial DNA together in a composition as recited in claim 1.

Applicants argue that the use of bacterial DNA as an adjuvant was known prior to the earliest priority date claimed by the instant application, and that the use of CpC motifs was known as demonstrated in Stacey et al. (reference YR and newly provided). Applicants note also that post-filing art demonstrates the use of CpG in generating an immune response. See Applicants' amendment, pages 17-19. Applicants' response and arguments have been fully considered, and not found persuasive. Initially, it is noted that post filing art shows the functionality of unmethylated CpG in DNA vaccines, which not disclosed in the instant

applications priority documents. Examiner does not contest that unmethylated CpG can be used as an adjuvant, rather the priority documents fail to teach or provide literal support for the instantly claimed invention. Even if one were to concede that the priority document provided support for the general use of bacterial DNA, it fails to antedate Kreig *et al.* as of its filing date and fails to provide the detailed guidance of '068. With respect to Tsang *et al.*, it is noted that Tsang *et al.* specifically teach the use of "CpG-rich synthetic DNA" (column 16), which the priority documents does not. Unlike the priority document which only provides the generally guidance to use bacterial DNA without any clear teaching to specific aspects of the bacterial DNA, Tsang *et al.* provide the specific guidance for the use of unmethylated DNA that was recognized in the art to be the adjuvant.

In summary, the priority documents provide general and specific guidance for various specific types of adjuvant, however, there is no literal nor figurative support that the use of CpG was contemplated. As noted previously, the priority documents relied upon by Applicants fail to adequately support the instantly claimed method. As noted in the previous office action, a later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In this case the prior applications provide support for the delivery of an antigen to a subject, however fail to provide literal or figurative support the instantly claimed invention as it is drawn to the delivery of DNA wherein an antigen is produced

by the cells of the subject. Thus, while the transdermal delivery of vaccines are supported in the prior applications, the specific combination of a non-bacterial DNA vaccines and the use of CpG from bacterial DNA as an adjuvant is not.

Claim Objections

The claims stand objected to because the restriction requirement is maintained with respect to the elected species of (ii) the adjuvant CpG. Applicants assert that the generic claim is allowable and argue that amendment to the claims is not required. See Applicants' amendment, page 16. Applicants' arguments have been fully considered, but not found persuasive.

As discussed below in detail, the generic claim has not been found allowable, therefore the claims should be amended to reflect the elected species of adjuvant.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99 and 102-136 stand rejected under 35 U.S.C. 102(e) as being anticipated by Tang *et al.* (US Patent 6,348,450 B1).

Applicants note that claims have been added to mirror the claims of Tsang *et al.* and argue that the priority date of the instant application is prior to that of Tsang et al. therefore the rejection should be withdrawn. See Applicants' amendment, pages 19-20. Applicants' arguments have been fully considered, but not found persuasive.

As discussed above, it is found that the priority date of the invention under examination is the filing date of the instant application. Accordingly, Tsang *et al.* qualifies as prior art. Applicants do not contest the basis of the teachings of Tsang *et al.* as anticipatory, noting that the claims have been added to mirror those of Tsang *et al.* for purposes of provoking an interference.

As stated previously, Tang *et al.* provide methods and materials for genetic immunization using DNA vectors. The methods taught by Tang *et al.* comprise a non-invasive method wherein the DNA vector is provided to the surface of the skin. Tang *et al.* provide general and specific guidance for the types of antigens to be expressed and specific guidance for the types of vectors for the expression. Tang *et al.* teach that vectors can be delivered alone, or in combinations with other agents that will aid in the transfection of a cell. Finally, Tang *et al.* teach that additional agents can be provided to augment the immune response, and specifically teach that CpG rich sequences can be used together with the transcription/translation signals necessary for expression (column 16, lines 25-36). The teachings of Tsang *et al.* anticipate the instantly claimed invention under examination.

Claims 1, 2, 4,14, 28, 30-44, 47-54, 80, 81, 87, 90, 93, 94, 96, 99, and 102-136 stand rejected under 35 U.S.C. 102(e) as being anticipated by Kreig *et al.* (US Patent 6,339,068).

Applicants argue that Kreig *et al.* does not specifically teach to use transdermal application for the purpose of inducing an immune response. See Applicants' amendment, pages 21-22. Applicants' arguments have been fully considered, but not found persuasive.

As stated in the previous office action, Kreig *et al.* teach methods and materials for immunization protocols for the delivery and expression of polynucleotide vectors. Examiner notes that Kreig *et al.* primarily details the use of CpG sequences as an adjuvant, and provides multiple context in which the CpG sequence can be used for genetic immunization. Clearly the teaching of Kreig *et al.* is for the use in immunization. It was noted in the basis of the rejection set forth in the previous office action that Kreig *et al.* teaches that transdermal delivery can be used for immunization relying and specifically citing methods provided in the references of Fynan, Tang, Fuller and Keller (column 10, lines 34-60). Kreig *et al.* provides detailed guidance on specific vectors and promoters, and various formulations for the delivery of the DNA vaccines.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99 and 102-136 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Khavari *et al.* (US Patent 6,087,341) in view of Krieg *et al.* ('068).

Applicants argue that neither Tsang *et al.* nor Kreig *et al.* qualify as prior art, therefore the rejection should be withdrawn. See Applicants' amendment, pages 22-23. Applicants' arguments have been fully considered, but not found persuasive.

As discussed above, each of Khavari *et al.* and Kreig *et al.* qualify as prior art of the instant invention. Moreover, it is noted that claims have been added to mirror those of both Khavari *et al.* and Kreig *et al.* for the purposes of provoking an interference. Claims 102-116 represent copies of claims 1-15 of Khavari *et al.*, however the elected species of adjuvant of CpG currently under examination is not taught by Khavari *et al.* Accordingly, Khavari *et al.* is not provided as a 102 type reference because it fails to teach all the limitations encompassed by the claim. However, Khavari *et al.* does teach transdermal methods of the delivery of polynucleotide vectors to generate an immune response in a subject. Khavari *et al.* teaches a variety of antigens and vectors that can be used, and provides various formulations for the transdermal delivery of the polynucleotide. In addition, Khavari *et al.* teach that other agents can be used to augment the immune response however Khavari *et al.* does not teach the use of CpG as an adjuvant. Kreig *et al.* teach methods and materials for immunization protocols for the

delivery and expression of polynucleotide vectors. Kreig *et al.* primarily detail the use of CpG sequences as an adjuvant, however provides multiple context in which the CpG sequence can be used for genetic immunization. Included in the methodology for delivery, Kreig *et al.* teaches that transdermal delivery can be used, however does not provide specific details on the practice of this methodology. It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the detailed teachings for transdermal delivery of a polynucleotide as taught by Khavari *et al.* to affect the methods of Kreig *et al.* One having ordinary skill in the art would have been motivated to use the methods of Khavari *et al.* because of the specific motivation provided by Kreig *et al.* to use transdermal delivery. There would have been a reasonable expectation of success to use the methods of transdermal delivery taught by Khavari *et al.* with the materials taught by Kreig *et al.* given the results of both Khavari *et al.* and Kreig *et al.* demonstrating the success of the methodology and materials detailed in each of the disclosures.

Thus, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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